REMARKS/ARGUMENTS

The Pending Claims

Claims 1 and 7-10, 12, 16-22, and 45-49 are pending and are directed to a method for inducing an immunological response against a malignant pancreatic cell in an individual (claims 1, 7-10, 12, 16-22, and 45-47) and a method for inhibiting growth of a malignant pancreatic cancer cell in an individual (claims 48 and 49).

Amendments to the Specification

The specification has been amended to correct a typographical error in paragraph 0052. Support for the amendment can be found in Figure 10. No new matter has been added by way of this amendment to the specification.

Amendments to the Claims

Claim 1 has been amended to clarify the claim language. Support for the amendments to claim 1 can be found in the specification at, for example, paragraphs 0049-0052, 0063, and 0066-0067.

Claims 45-49 are new. Claims 46 and 47 recite that the immunological response is a cell-mediated immune reaction as supported by the specification at, for example, paragraphs 0012 and 00106. New claim 48 recites a method for inhibiting growth of a malignant cancer cell in an individual as supported by the specification at, for example, paragraph 00107.

Claims 45 and 49 recite that the one or more DNA segments comprise SEQ ID NO: 1 and SEQ ID NO: 3 or encode SEQ ID NO: 2 and SEQ ID NO: 4. SEQ ID NOs: 1 and 2 correspond to the nucleic acid and amino acid sequences, respectively, of wMUC-1(6) (see, e.g., paragraphs 0049-0050, 0067, 00203, and 00208). SEQ ID NOs: 2 and 4 correspond to the nucleic acid and amino acid sequences, respectively, of wCEA(6D) (see, e.g., paragraphs 0051-0052, 0063, 00203, and 00208).

No new matter has been added by way of these amendments to the claims.

Summary of the Office Action

The Office rejects 1, 7-10, 12, 13, and 16-22 under 35 U.S.C. § 103(a) as allegedly obvious in view of Laidlaw et al. (U.S. Patent 7,273,605), Pecher (WO 01/24832), and Kotera et al. (*Cancer Res., 54(11)*: 2856-2860 (1994)).

Reconsideration of the rejection is hereby requested.

Discussion of Obviousness Rejection

The Office maintains that the subject matter of the pending claims is obvious in view of the Laidlaw, Pecher, and Kotera references. The obviousness rejection is traversed for the following reasons.

For subject matter defined by a claim to be considered obvious, the Office must demonstrate that the differences between the claimed subject matter and the prior art "are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains." 35 U.S.C. § 103(a); see also *Graham v. John Deere Co.*, 383 U.S. 1, 148 U.S.P.Q. 459 (1966). The ultimate determination of whether an invention is or is not obvious is based on certain factual inquiries including: (1) the scope and content of the prior art, (2) the level of ordinary skill in the prior art, (3) the differences between the claimed invention and the prior art, and (4) objective evidence of nonobviousness. *Graham*, 383 U.S. at 17-18, 148 U.S.P.Q. at 467.

Consideration of the aforementioned *Graham* factors here indicates that the present invention, as defined by the pending claims, is unobvious in view of the cited references.

As regards the scope and content of the prior art, the Office contends that the Laidlaw reference discloses a method comprising administering a priming composition (which comprises a first non-replicating viral vector) and a boosting composition (which comprises a second non-replicating viral vector) to a subject to treat and/or prevent a cancer. The Office contends that the Laidlaw reference teaches that the viral vector can comprise a nucleotide of interest that encodes a disease associated antigen, and the antigen may be one that is recognized by the immune system after disease (e.g., cancer). The Office contends that the

Laidlaw reference teaches that immunization of mice using a heterologous prime/boost protocol with two different vectors encoding multiple antigens (i.e., the MEI polypeptide which comprises epitopes from a viral antigen and murine tumor antigens) resulted in an improved immune response over homologous immunization with either vector alone.

The Office contends that the Laidlaw reference discloses that colon and breast cancer antigens include CEA and MUC-1. The Office acknowledges that the Laidlaw reference does not disclose the administration of a first and second vector each containing one or more DNA segments encoding CEA and MUC to produce an immunological response against a malignant pancreatic cell.

The Office relies on the Pecher reference for its disclosure of a pharmaceutical composition for treating and preventing human tumors, which tumors express CEA and/or MUC-1, and the use of the pharmaceutical composition as a vaccine for activating the immune system.

The Office relies on the Kotera reference for its disclosure of a tandem repeat epitope of human MUC-1 in sera from pancreatic cancer patients.

For purposes of the analysis here, and for the sake of argument, the level of ordinary skill can be considered to be relatively high, such that a person of ordinary skill in the art would have an advanced degree and/or several years of experience in the relevant field.

The present invention, as defined by the pending claims, is directed to a method for inducing an immunological response against a malignant pancreatic cell in an individual, wherein the method comprises (a) selecting an individual having malignant pancreatic cells or at risk for developing such a pancreatic tumor, (b) administering to the individual a first poxvirus vector containing one or more DNA segments that encode (i) CEA, an antigenic portion thereof, or a modified version thereof, and (ii) MUC, an antigenic portion thereof, or a wobbled version thereof, and (c) at regular intervals thereafter administering at least a second poxvirus vector containing one or more DNA segments that encode (i) CEA, an antigenic portion thereof, or a modified version thereof, and (ii) MUC, an antigenic portion thereof, or a wobbled version thereof, such that an immunological response against the malignant pancreatic cell is induced in the individual.

Additionally, the present invention, as defined by the pending claims, is directed to a method for inhibiting growth of a malignant pancreatic cell in an individual, wherein the method comprises (a) selecting an individual having malignant pancreatic cells or at risk for developing such a pancreatic tumor, (b) administering to the individual a first poxvirus vector containing one or more DNA segments that encode (i) CEA, an antigenic portion thereof, or a modified version thereof, and (ii) MUC, an antigenic portion thereof, or a wobbled version thereof, and (c) at regular intervals thereafter administering at least a second poxvirus vector containing one or more DNA segments that encode (i) CEA, an antigenic portion thereof, or a modified version thereof, and (ii) MUC, an antigenic portion thereof, or a wobbled version thereof, such that the growth of the malignant pancreatic cell is inhibited in the individual.

None of the cited references, when considered alone or in combination, teaches or suggests a prime/boost protocol comprising a first and second poxvirus vector containing one or more DNA segments that encode (i) CEA, an antigenic portion thereof, or a modified version thereof, and (ii) MUC, an antigenic portion thereof, or a wobbled version thereof, for inducing an immune response against a malignant pancreatic cell or inhibiting the growth of a malignant pancreatic cell, as required by the pending claims.

While the Laidlaw reference provides an example of a heterologous prime/boost protocol with two different vectors encoding the MEI polypeptide (which comprises epitopes from a viral antigen and murine tumor antigens), the Laidlaw reference does not disclose a prime/boost protocol with two different vectors encoding both CEA and MUC for inducing an immune response against a malignant pancreatic cell or inhibiting the growth of a malignant pancreatic cell, as required by the pending claims. Furthermore, the Laidlaw reference does not disclose that CEA or MUC are pancreatic tumor antigens. The deficiencies of the Laidlaw reference are not remedied by the Pecher or Kotera references.

The Pecher reference discloses a pharmaceutical composition comprising one vector (e.g., a plasmid) comprising the gene encoding MUC-1 and/or another vector (e.g., a plasmid) comprising the gene encoding CEA (see Abstract). Thus, CEA and MUC-1 are not in the same vector as required by the pending claims. Additionally, the Pecher reference does not identify CEA and/or MUC-1 as pancreatic cancer associated antigens, or disclose the administration of a first and a second vector containing one or more DNA segments encoding

CEA and MUC-1 to induce an immunological response against a malignant pancreatic cell or inhibit growth of a malignant pancreatic cell, as required by the pending claims.

Applicants further note that the Pecher reference does not disclose any working examples wherein the vector encoding CEA and the vector encoding MUC-1 are administered together. Instead, the Pecher reference describes an experiment wherein an adenovirus vector encoding MUC-1 is administered to a mouse followed by administration 14 days later of a plasmid encoding MUC-1. In other words, in the only experiment described in the Pecher reference, a vector encoding only one tumor associated antigen (MUC) was used. Thus, the Pecher reference provides no evidence that the administration of a vector encoding CEA and a vector encoding MUC-1 would result in the treatment and prophylaxis of human tumors.

The Kotera reference identifies a tandem repeat epitope of human MUC-1 in sera from pancreatic cancer patients. The Kotera reference does not disclose a vector encoding MUC-1, much less a first and second vector containing one or more DNA segments encoding CEA and MUC-1, or the administration of the first and second vectors to produce an immunological response against a malignant pancreatic cell, as required by the pending claims. Furthermore, the Kotera reference does not disclose that CEA is a pancreatic tumor antigen.

Accordingly, none of the cited references teaches or suggests that CEA is a pancreatic tumor antigen or that the administration of a vector encoding both CEA and MUC could be used to induce an immunological response against a malignant pancreatic cell or inhibit the growth of a pancreatic cell in an individual.

As discussed in the previous Reply to Office Action, the prior art (e.g., Palmowski et al., *J. Immunol., 168*: 4391-4398 (2002) and Brody et al., *Immunol., 22*: 75-85 (1972)) disclosed that the administration of two or more antigens together (at the same location) could result in competition between the antigens resulting in a reduced immune response. Thus, one of ordinary skill in the art would not have known without practicing undue experimentation whether the administration of a vector encoding both CEA and MUC could be used to successfully induce an immunological response (e.g., against a malignant

pancreatic cell) or inhibit the growth of a pancreatic cell in a individual. Furthermore, since the cited references did not disclose that CEA was a pancreatic tumor antigen, one of ordinary skill in the art would have had no reason to administer CEA, an antigenic portion thereof, or a modified version thereof (e.g., in a prime/boost protocol with MUC as in the claimed invention) in order to induce an immunological response against a malignant pancreatic cell or inhibit the growth of a pancreatic cell in a individual.

The Office cites to Aarts et al., *Cancer Res., 20*: 5770-5777 (2002), as evidence that simultaneous expression of multiple antigens from a DNA vector-based vaccine for an antitumor immune response was known in the art. In particular, the Office contends that the Aarts reference describes recombinant poxviruses containing the human CEA gene and the murine B7.1, ICAM-1, and LFA-3 genes. Applicants note that the vectors to which the Office points in the Aarts reference only express one antigen (CEA). B7.1, ICAM-1, and LFA-3 are co-stimulatory molecules, which are used to increase an immune response to an antigen (in this case, CEA). The specification describes such co-stimulatory molecules at, for example, paragraphs 0034 and 0071. Thus, the Aarts reference does not disclose simultaneous expression of multiple antigens.

Even if the combination of the disclosures of the cited references are considered to properly establish *prima facie* obviousness, the existence of unexpected benefits attendant the present invention rebut the obviousness position recited in the Office Action.

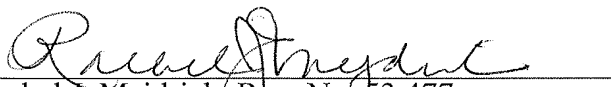
Clinical studies were performed to determine the effect of administering a vaccine comprising a first and second vector containing CEA and MUC-1, which antigens were found on over 90% of pancreatic tumors (see Examples 4, 5, and 11 of the specification). As a result, metastatic pancreatic cancer patients receiving this vaccine were shown to have a trend toward an overall survival *greater than the expected* median overall survival (see Abstract of Schuetz et al., *J. Clin. Oncol., 2005 ASCO Annual Meeting Proceedings, 23(16S Part I of II in June 1 Supplement)*: 2576 (2005)). The unexpected beneficial results demonstrate that the inventive methods successfully can be used to induce an immunological response against malignant pancreatic cells and inhibit the growth of pancreatic cells in pancreatic cancer patients.

Considering all of the *Graham* factors together, it is clear that the present invention – as defined by the pending claims – would not have been obvious to one of ordinary skill in the art at the relevant time in view of the combined disclosures of the Laidlaw, Pecher, and Kotera references. Accordingly, the obviousness rejection should be withdrawn.

Conclusion

Applicants respectfully submit that the patent application is in condition for allowance. If, in the opinion of the Examiner, a telephone conference would expedite the prosecution of the subject application, the Examiner is invited to call the undersigned agent.

Respectfully submitted,



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